CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 83232

PRINTED LABELING

HYDROCHLOROTHIAZIDE TABLETS

DESCRIPTION

Hydrochlorothiazide is the 3,4-dihydro derivative of chlorothiazide. Its chemical name is 6-chloro-7-sulfamyl-3, 4- dihydro-1, 2, 4-benzothiadiazine-1,1-dioxide. It is a white or practically white crystalline compound with low solubility in water, but is readily soluble in dilute aqueous sodium hydroxide.

ACTION

The mechanism of action results in an interference with the renal tubular mechanism of electrolyte reabsorption. At maximal therapeutic dosage all thiazides are approximately equal in their diuretic potency. The mechanism whereby thiazides function in the control of hypertension is unknown.

INDICATIONS

Hydrochlorothiazide is indicated as adjunct therapy in edema associated with congestive heart failure, hepatic cirrhosis and corticosteroid and estrogen therapy.

Hydrochlorothiazide has also been found useful in edema due to various forms of renal dysfunction as:

Nephrotic syndrome;
Acute glomerulonephritis; and
Chronic renal failure.

Hydrochlorothiazide is indicated in severe edema when due to pregnancy. (See "Contraindications" and "Warnings" below.)

Diuretics are indicated in the management of hypertension either as the sole therapeutic agent or to enhance the effect of other antihypertensive drugs in the more severe forms of hypertension of pregnancy.

The drug is also indicated in toxemia of pregnancy (eclampsia); angina due to congestive heart failure and/or hypertension; and "drug induced" edema.

CONTRAINDICATIONS

Anuria.

Hypersensitivity to this or other sulfonamide derived drugs.

The routine use of diuretics in an other-wise healthy pregnant woman with or with-out mild edema is contraindicated and possibly hazardous.

WARNINGS

Should be used with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

USAGE IN PREGNANCY

Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

NURSING MOTHERS

Thiazides cross the placental barrier and appear in cord blood and breast milk.

PRECAUTIONS

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals.

All patients receiving thiazide therapy should be observed for clinical signs of fluid or electrolyte imbalance; namely hyponatremia, hypochloremic alkalosis and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs, irrespective of cause are: Dryness of mouth, thirst, weakness, lethargy drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH.
Interference with adequate oral electrolyte intake will also contribute to hypokalemia.
Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt except in rare instances when the hyponatremia is life threatening. In actual salt depletion appropritate replacement is the therapy of choice.
Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy.
Insulin requirements in diabetic patients may be increased, decreased or unchanged. Latent diabetes mellitus may become manifest during thiazide administration. Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This diminution is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.
If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy.
Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

ADVERSE REACTIONS

A. GASTROINTESTINAL SYSTEM REACTIONS:
1. anorexia
2. gastric irritation
3. nausea
4. vomiting
5. cramping
7. constipation
8. jaundice (intrahepatic cholestatic jaundice)
9. pancreatitis

B. CENTRAL NERVOUS SYSTEM REACTIONS
1. dizziness
2. vertigo
3. parasthesias
4. headache
5. xanthopsia

C. HEMATOLOGIC REACTIONS
1. leukopenia
2. agranulocytosis
3. thrombocytopenia
4. aplastic anemia

D. DERMATOLOGIC-HYPERSENSITIVITY REACTIONS
1. purpura
2. photosensitivity
3. rash
4. urticaria
5. necrotizing angiitis (vasculitis) (cutaneous vasculitis)

E. CARDIOVASCULAR REACTION
Othostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics.

F. OTHER

1. hyperglycemia
2. glycosuria
3. hyperuricemia
4. muscle spasm
5. weakness
6. restlessness

Whenever adverse reactions are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

DOSAGE AND ADMINISTRATION

Therapy should be individualized according to patient response. This therapy should be titrated to gain maximal therapeutic response as well as the minimal dose possible to maintain that therapeutic response.

Diuretic - 25 to 200 mg.

Antihypertensive - 25 to 100 mg.

Pediatric - Under 6 months 10 to 15 mg./lb./day

HOW SUPPLIED

Hydrochlorothiazide tablets are supplied as 50 mg. tablets in bottles of 100 and 1000.

Danbury

NDC-0591-5324-04

HYDROCHLOROTHIAZIDE
TABLETS U.S.P.
50 mg.
YELLOW

CAUTION: Federal law prohibits dispensing without prescription.

1000 TABLETS

DANBURY PHARMACAL, INC.
Danbury, Conn. 06810

Each tablet contains:
Hydrochlorothiazide 50 mg.

Average dose; see accompanying brochure.

See accompanying brochure for complete prescribing information.

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JAN 24 1975

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